Severe allergic reaction induced by dexlansoprazole: a case report and literature review

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Background

- **Proton pump inhibitors** (PPIs) are one of the most worldwide prescribed drugs. The prevalence of PPIs users was of 21,5% in Quebec in 2010.
- **Dexlansoprazole** belongs to the new generation of PPIs and was marketed in Canada in 2010.

We report a case of hypersensitivity (HS) with dexlansoprazole

Literature review

- **1. (ADR) online databases of governments**: Health Canada (HC) database, Federal Food and Drug Administration Adverse Events Reporting System (FAERS) public dashboard and Eudravigilance of European Medicine Agency (EMA)

⇒ **Dates**: data available until Jan 11th, 2019

⇒ **Keywords**: "Dexlansoprazole"

⇒ **Results**: 0 case in HC and EMA, **6 cases** of drug HS included 1 serious case on FAERS

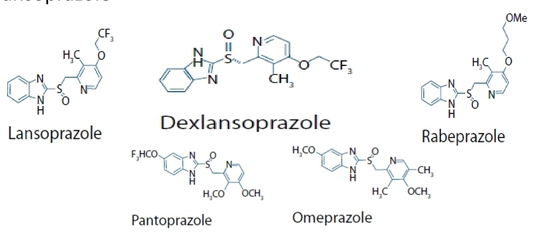
- **2. Embase, Pubmed, and CINAHL:**

⇒ **Dates**: Jan 11th, 2019

⇒ **Keywords**: "Anaphylaxis", "Hypersensitivity", "Drug Hypersensitivity Syndrome" and "Dexlansoprazole" and "Proton Pump Inhibitors"

⇒ **Results:**

- **0 case of HS with the dexlansoprazole** is found
- Around 90 case reports are found with all PPIs
- HS with lansoprazole is one of the most described one
- **Cross reactivities** with IPP is frequent and seem to be linked with the pyridine central ring
- **Selective allergies** of dexlansoprazole, lansoprazole and rabeprazole seem to be linked to their side chains
- **Dexlansoprazole = R-enantiomer of lansoprazole** provides 3 to 5 times greater Cmax and has a **higher dosage** than lansoprazole



Case description

PATIENT MEDICAL HISTORY

- ADR: **allergic reaction**
- Suspected drug: **dexlansoprazole 60mg**, oral ingestion, one single dose
- Time of onset of symptoms: **15 minutes post dose**
- Chronology of symptoms:
  - **Burning sensations** in both feet and hands
  - **Vomitings**
  - **Coalescing maculopapular rash** on almost 100% of body surface
  - **Swelling of face and tongue**
  - **Blackouts**

PATIENT

24-year-old ♀
Canadian caucasian
65Kg/165cm

TREATMENTS

- **1.** Medication given **at patient home**: Salbutamol → **Patient airways remains secured**
- **2.** Intraveinous shots given **in the emergency room**: IV dyphenhydramine, IV methylprednisolone, IV famotidine and IV ondansetron
- **3.** Prescription given **at hospital discharge**: oral prednisone 20mg 3x/day, oral diphenhydramine 50mg 3x/day, oral famotidine 20mg twice/day and s/c epinephrine 0,3mg if needed

→ **The patient completely recovered and was discharged after a four hours observation**

Table 1. Naranjo algorithm - ADR probability Scale

Questions	Yes	No	Do not know	Score
1. Are there previous conclusive reports on this reaction?	+1	0	0	1
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	2
3. Did the adverse event improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	1
4. Did the adverse event reappear when the drug was readministered?	+2	-1	0	0
5. Are there alternative causes that could on their own have caused the reaction?	-1	+2	0	2
6. Did the reaction reappear when a placebo was given?	-1	+1	0	0
7. Was the drug detected in blood or other fluids in concentrations known to be toxic?	+1	0	0	0
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	0
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	1
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	1

Total Score of 8: Probable imputability of dexlansoprazole

References

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Assessment of causality

- **Primary exposure with dexlansoprazole:**

⇒ When?: Two months before

⇒ What?: Primary exposure led to burns in hands and feet in 15 minutes post dose

⇒ Treatment?: This previous reaction was resolved in 30 minutes without any treatment

- **Naranjo algorithm**: (Table 1)
- **Dermatological tests**: (Picture 1)

⇒ Oral drug provocation test to pantoprazole 40mg (december 2018): DPT was considered negative by the absence of clinical signs and the absence of a 20% fall in FEV1

⇒ Skin prick tests (SPT): *+: positive reaction; -: negative reaction*

- ***SPT1. February 2018:*** **60mg dexlansoprazole (+)**, 15mg lansoprazole (-)
- ***SPT2. December 2018*****:** 60mg dexlansoprazole (-), 30mg lansoprazole (-) and 40mg pantoprazole (-)
- ***SPT3. January 2018:*** 30mg et 60 mg dexlansoprazole (-), 15mg lansoprazole (-), 40mg pantoprazole (-) and 20mg omeprazole (-)

- **Analysis of ingredients:** (Table 2)

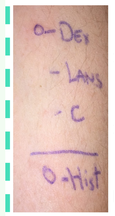
⇒ Excipients and mainly coloring agents are known to be potential allergens

⇒ FD&C Blue No. 2 is associated with rare case of pruritic skin disorders

No conclusion on the imputability of the excipients can be drawn at this time

Table 2. dexlansoprazole Dexilant ingredients

Inactive ingredients of the enteric-coated granules	Sugar spheres, magnesium carbonate, sucrose, low-substituted hydroxypropyl cellulose, titanium dioxide, hydroxypropyl cellulose, hypromellose 2910, talc, methacrylic acid copolymers, polyethylene glycol 8000, triethyl citrate, polysorbate 80, colloidal silicon dioxide
Inactive ingredients of the capsule shell	Hypromellose, carrageenan and potassium chloride, titanium dioxide, **FD&C Blue No. 2 aluminium lake (blue capsule shell—30 and 60mg capsules), black ferric oxide (gray capsule shell—30mg capsule)**



Picture 1. February 2018 - Skin prick tests results after 20 minutes

⇒ **Dexlansoprazole 60 mg capsule skin prick test is considered positive with a wheal reaction with a mean diameter of 3 mm**

⇒ **One year later: dexlansoprazole 30 and 60 mg capsules skin prick tests are negative (not displayed)**

Legend: Dex: dexlansoprazole; Lans: lansoprazole; C: negative control; Hist: histamine positive control;

Importance to practictioners

We report an anaphylactic reaction with 60mg dexlansoprazole. To our knowledge, this is the first case report concerning anaphylactic reaction with dexlansoprazole in the literature.

In view of the skin prick tests results (positive only with the 60 mg capsule and negative one year later), we cannot exclude false negative prick tests with dexlansoprazole one year after exposure (neither than with others PPIs). Contribution of excipients (e.g. FD&C Blue No. 2 aluminium lake) cannot be excluded either. No rechallenge was done with isolated coloring agents to validate this hypothesis. Finally, drug hypersensitivities can disappeared with time. It is important to report unexpected/emerging adverse drug reactions to better support patient care.

Contact: jean-francois.bussieres@ssss.gouv.qc.ca - **Conflict of interest:** None - **Fundinhsjg**: None

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